REMARKS:

The following remarks are submitted as a full and complete response to the Office Action issued on January 4, 2010. Applicants note that the Patent Office has withdrawn the previous anticipation rejections under 35 U.S.C. §102(a) based on Cha (2005). The Patent Office has also withdrawn the rejection of claims 4 and 8 under 35 U.S.C. § 102(b) based on Yoon (200) and the rejections of claims 1, 3 and 5-6 under 35 U.S.C. 103(a) over Yoon (2000) in view of U.S. 5,976,567. Claims 1, 3 and 5-6 are pending. Reconsideration of all outstanding rejections is respectfully requested in view of the foregoing amendment and following remarks.

Claim Rejections Under 35 U.S.C. §103

The Patent Office has rejected claims 1, 3 and 5-6 under 35 U.S.C. §103(a) as obvious over Yoon et al. ("Yoon"), "Pregnancy and Delivery of Healthy Infants Developed From Vitrified Oocytes in a Stimulated In Vitro Fertilization-Embryo Transfer Program," Fertility and Sterility, Vol. 74, No. 1, July 2000, pp. 180-181, in view of Wheeler et al. (U.S. Patent No. 5,976,567)("Wheeler") and further in view of Martino et al. ("Martino"), "Development into Blastocysts of Bovine Oocytes Cryopreserved by Ultra-Rapid Cooling," Biology of Reproduction, Vol. 54, pp. 1059-1069, 1996. The Patent Office asserts that "with regards to the use of gold grids, the difference between that claim and that taught in the art amounts to no more than a simple substitution of one known equivalent for another to obtained predictable results." Moreover, the Patent Office alleges that one would have been motivated to alter the freezing rate of human

oocytes by use of slush nitrogen in place of liquid nitrogen by Yoon because Martino taught that "different sized oocytes would be affected differently from different rates of cooling." Applicants respectfully traverse this rejection.

The Patent Office admits that Yoon did not teach use of a gold grid or use of nitrogen slush in vitrification of human oocytes. However, relying on Wheeler that allegedly teaches using a gold grid to vitrifying vesicles thereon, the Patent Office contends that it would have been a mere matter of design choice to the skilled artisan to choose a gold grid from amongst the many well-known choices of grids for use in vitrification. Again, Wheeler, which teaches a method for the preparation of liquid-nucleic acid particles, involves completely different technology from that involved in the present application. Moreover, Wheeler does not even mention oocytes, let alone vitrification or devitrification of oocytes. In fact, until the present application, copper is the only grid that was known for being used for vitrification of oocytes, especially human oocytes. Therefore, Applicants respectfully submit that one skilled in the art would not have been motivated to use a gold grid from the teaching of Wheeler in vitrifying human oocytes as described in Yoon in view of different technology involved therein.

With respect to nitrogen slush, the Patent Office acknowledges that neither Yoon nor Wheeler teaches or suggests using nitrogen slush for vitrifying human oocytes. Then, the Patent Office relies on the teaching of Martino to cure this deficiency.

In particular, the Patent Office asserts that "Martino taught that rapid cooling can have damaging effects on oocytes and the damage that occurs is species specific ... Martino suggests that some species might freeze better in slush while other would fare better in liquid nitrogen." Office Action at pages 3-4. Applicants respectfully submit that

nowhere does Martino teach or suggest that the damage effects of rapid cooling on oocytes can be "species specific" or that some species might freeze better in slush nitrogen. What Martino teaches or suggests are that (1) both bovine oocytes and *Drosophila* embryos have high chilling sensitivity compared to mouse embryos; and that (2) because of this difference in chilling sensitivity, ultra rapid cooling is used to successfully vitrify bovine oocytes or *Drosophila* embryos while conventional cooling produces successful results in vitrifying mouse embryos. Martino at page 1059 and 1060, right column and abstract. However, according to Martino, in both ultra rapid cooling and conventional cooling, liquid nitrogen is used. Id. Nowhere does Martino teach or suggest that using slush nitrogen or liquid nitrogen can produce different results in vitrification of oocytes or embryos depending on species. Thus, Marino lacks any teaching or suggestion that would have led or motivated one skilled in the art to choose slush nitrogen over liquid nitrogen depending on species, let alone in vitrification of human oocytes in particular.

Instead, as described in the specification, Martino shows that using slush nitrogen for ultra rapid cooling of bovine oocytes is inferior to using liquid nitrogen in terms of survival rate of vitrified bovines oocytes and cleavage and blastocyst formation. Specification at page 2, paragraphs [5] and [6]. The comparative results of cryopreservation of bovine oocytes between using slush nitrogen and liquid nitrogen are shown in Fig. 4 of Martino. These results clearly demonstrate the significant differences in cryopreservation between using slush nitrogen and liquid nitrogen. That is, Fig. 4 shows that in all of three observations, *i.e.,* morphological survival rate, cleavage and blastocyst formation, cryopreservation of bovine oocytes using slush nitrogen produces

inferior results than that using slush nitrogen. In fact, Martino itself acknowledges this difference as "significant." Martino, in Fig. 4. Therefore, Martino would have discouraged or taught away one skilled in the art from using slush nitrogen in vitrifying oocytes. As such, the totality of the disclosure of Martino consistently disfavors using slush nitrogen in vitrifying oocytes, which would have certainly mitigated a reasonable expectation of success that one skilled in the art would have in terms of using slush nitrogen in vitrifying oocytes. Therefore, Applicants respectfully submit that one skilled in the art would not have been motivated to use slush nitrogen in the method disclosed in Yoon to arrive at the claimed method with a reasonable expectation of success.

However, Applicants surprisingly found that when nitrogen slush was used instead of liquid nitrogen for vitrifying human oocytes, the survival rate of vitrified human oocytes was significantly increased and the apoptosis after thawing was significantly decreased. Specification, at page 2, paragraph [6]. As explained in the previous amendment filed on June 1, 2009, these findings are fully supported by working examples and drawings of the present application. See the June 1, 2009 amendment at page 7.

Given the state of knowledge of one skilled in the relevant art at the time of the invention including the teaching against using nitrogen slush for vitrifying oocytes, it would not have been reasonably expected that using nitrogen slush in vitrifying human oocytes would result in such a significant improvement in survival rate of vitrified oocytes and cleavage and blastocyst formation. Thus, Applicants respectfully submit that these significant improvement in vitrifying human oocytes achieved by the claimed

method certainly qualifies as unexpected results, which is sufficient to rebut any *prima facie* case of obviousness even if it was established.

Accordingly, Applicants respectfully submit that the claimed invention would not have been obvious to one skilled in the art from the teachings of Yoon, Wheeler and Martino, alone or in combination, and thus reconsideration and withdrawal of this rejection are respectfully requested.

In light of the foregoing, Applicants submit that all outstanding rejections have been overcome, and the instant application is in condition for allowance. Thus, Applicants respectfully request early allowance of the instant application. The Commissioner is hereby authorized to charge any fees or credit any overpayment to Deposit Account No. 02-2135.

Respectfully submitted,

By _____

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